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This Week's Citation Classic

Dausset J. Iso-leuco-anticorps. *Acta Haematol.* **20**:156-66, 1958.
[Centre National de Transfusion Sanguine, Paris, France]

This paper provides a description of the first human leucocyte (tissue) group. Polytransfused patients' sera agglutinated some but not all leucocytes. This group, initially called 'Mac,' is now known as HLA-A2. This work opened up the understanding of the human major histocompatibility complex HLA, a key to the immune system. [The *SCI*® indicates that this paper has been cited in over 165 publications since 1961, making it the 5th most-cited paper ever published in this journal.]

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"In 1952, when only the red blood cell groups were known, I mixed on a glass plate the serum of an agranulocytic woman with the bone marrow of another individual. I observed a massive macroscopic agglutination. I soon understood that it was not due to autoantibodies but to alloantibodies (at that time called isoantibodies).

"This paper gathered together all the work that had been done since 1952, in collaboration with Gilbert Malinvaud, Hélène Brécy, and later, Jacques and Monique Colombani (This work was also described in a book [1])

"During this time, we organised the systematic detection of leucoantibodies in the sera of polytransfused patients tested against a panel of leucocytes from volunteers from the National Blood Transfusion Centre. The agglutinations were sometimes obvious and sometimes weak, of very dubious reproducibility There were no computers at that time and our results were exposed on a large poster on the laboratory wall. We almost lost hope of ever making sense of it, so numerous were the different patterns. However, we noticed, after numerous repetitions, that the leucocytes from three panel donors were less often agglutinated than others. This gave us the idea that they lacked a certain antigen which is otherwise frequent in the population. Six sera did not agglutinate these three individuals, but agglutinated **11** others, thus dividing the population into two groups: one bearing the Mac antigen (not a Scottish name, but the initials of the surnames of the three non-agglutinated individuals) and the other without this antigen. An important fact was that these sera were unable to agglutinate their own leucocytes (they were not autoantibodies) nor the leucocytes of the other patients who produced similar antibodies.

"Formal proof was obtained when we observed that among the patients systematically transfused with Mac-positive blood, only the Mac-negative recipients developed an anti-Mac antibody.

"These leucocyte antigens are genetically determined since the pattern of agglutination with a battery of anti-leucocyte sera was strictly identical in monozygotic twins and different in dizygotic twins. Lastly, we demonstrated that leucocyte antibodies were responsible for the transfusion reactions.

"Thus, this work gathers together all the principles and first fruits of leucocyte immunohaematology. This was the starting point of an extraordinary biological adventure and is the reason why this paper has been highly cited. Two laboratories followed in our footsteps: J.J. Van Rood soon afterward described a supertypic antigen, 4a4b (Bw4,Bw6);[2] Rose Payne with W. Bodmer described the first two alleles, LA1 and LA2 (LA2 being identical to Mac).[3]

"Soon there were more than three musketeers: B. Amos, R. Ceppellini, F. Kissmeyer-Nielsen, P. Terasaki, and R. Walford joined the game, rapidly followed by numerous scientific communities. A unique collaborative research study was undertaken and has continued ever since. Thanks to ambitious international workshops which allow the exchange of reagents and information, the extraordinary skein of the human HLA complex was unraveled.[4-10] Its essential role in transplantation and, generally speaking, in immunology is well known, as well as its association with numerous diseases.

"Starting with the first serological data, it has been possible, in the space of 20 years, to decipher the biological composition and function of these molecules, protruding like antennae from the surface of our cells. We are now beginning to study the genes which govern these cells, and can expect still more marvels to come."

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4. **Videbiek A,** ed. *Histocompatibilily testing. 1965.* Copenhagen: Munksgaard, 1965. 4288 p.
5. **Curtoni E S. Mattiuz P L & Tosi R M.** eds. *Histocompatibility testing. 1967.* Copenhagen: Munksgaard. 1967. 458 p.
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8. **Kissmeyer-Nielsen F,** ed. *Histocompatibilily testing. 1975.* Copenhagen: Munksgaard. 1975. 1035 p.
9. **Bodmer W F. Batchelor J R, Bodmer J G. Festenstein H & Morris P J,** eds. *Histocompatibilily testing. 1977.* Copenhagen: Munksgaard. 1977. 612 p.
10. **Terasaki P I,** ed. *Histocompatibility testing. 1980.* Los Angeles. CA: UCLA Tissue Typing Laboratory. 1980. 1227 p.